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DEPARTMENT OF HEALTH & HUMAN SERVICES
New York District
Food & Drug Administration
158-15 Liberty Avenue
Jamaica, NY 11433

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Philip J. Zellner
President
Z Cosmetica USA, LLC
1650 New Highway
Farmingdale, NY 11735

June 28, 2004

Ref: NYK-2004-20

Dear Mr. Zellner:

During an inspection of your drug manufacturing facility located in Farmingdale, New York, conducted between the dates of March 5 and 19, 2004, our investigators documented deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211). Such deviations cause your drug products, such as, hydrocortisone cream, benzyl peroxide gel, salicylic acid gel, hydroquinone cream, and coal tar shampoo to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act as follows:

1. Failure to test or examine, as appropriate, each lot of components, drug product containers and closures. [21 CFR 211.84(d)] Specifically, the firm does not test or examine each lot of components, drug product containers or closures.

2. Failure to test each batch of drug product to determine conformance with final specifications. [21 CFR 211.165(a)] Specifically, the firm does not test each batch of drug product to determine conformance with final specifications.

3. Failure to establish written procedures for production and process control designed to assure that drug products have the identity, strength, quality and purity that they are represented to possess. [21 CFR 211.100(a)] Specifically, there are no written standard operating procedures for component controls, production and process controls, labeling and packaging controls, and laboratory controls. Also, process validation has not been conducted for any of the firm's drug products.

4. Failure to develop a written testing program to test the stability characteristics of drug products. Failure to establish stability testing data in determining an appropriate expiration date for drug products. [21 CFR 211.166(a) and (b)] Specifically, the firm does not collect stability samples or test the stability of their drug products.

5. Failure to establish procedures designed to prevent microbiological contamination of drug products not required to be sterile. [21 CFR 211.113(a)]. Specifically, the deionized water system used to manufacture purified water for drug products has not been qualified and procedures have not been established to ensure prevention of microbial contamination. In addition, the lack of control in the water system has led to practices such as allowing a point-of-use hose on the DI water system to remain in a bucket of standing water when not in use.

6. Failure to establish and follow written procedures for cleaning and maintenance of equipment. [21 CFR 211.67(b)] Specifically, the investigator noted that a stock pile of plastic empty drums, mostly of a 5 gallon capacity, contained a residue on the inside of the container. This residue remained embedded on the inner surfaces even after the pails had been cleaned. These drums are used without liners, are not dedicated and are repeatedly reused to hold batches of different products. The drums are utilized as in-process and storage containers for compounded products prior to filling. Also, the investigator observed that an empty, uncovered mixing tank had an orange/brown colored residue along the inside bottom of the tank. The firm had indicated that this tank was the main mixing equipment used during drug batch production. This tank was equipped with a portable Lightening mixer that was mounted directly above the tank on a block of bare wood; the paint on the motor housing was peeling off.

   In addition, there are no written procedures detailing the use and maintenance of the deionized (DI) water system. Routine monitoring and maintenance of the DI water system is not documented. This water system purports to supply purified water that is used in the manufacture of the firm's drug products. The only in-line service indicator on the water system was not operational.

7. Failure to establish a quality control unit that shall have the responsibilities as identified in 21 CFR 211.22. Specifically, the firm does not have a Quality Control Unit.

8. Failure to maintain individual equipment logs as a written record of equipment cleaning, maintenance and use. [21 CFR 211.182] Specifically, the firm does not maintain equipment cleaning and usage logs or cleaning procedures.

9. Failure to include in batch production records complete information relating to the production and control of each batch. [21 CFR 211.188] Batch records, such as, for Hydroquinone Cream 4% lot # 3L13 and Benzoyl Peroxide Gel 10% lot # 3E01 do not include manufacturing procedures and documentation of processing steps actually conducted. Also, the firm does not have batch production records for every drug product. In some instances, verbal manufacturing instructions are given to the manufacturing staff.

10. Failure to test in-process materials for identity, strength, quality, and purity as appropriate. [21 CFR 211.110(c)] Specifically, the firm does not test in-process materials for identity, strength, quality, and purity.

11. Failure to formulate batches with the intent to provide not less than 100 percent of the labeled or established amount of active ingredient. [21 CFR 211.101(a)]. Due to a formulation error on the master production record for Benzoyl Peroxide Gel, batches 3E01 and 3H03 were formulated to contain only 93.6% of the declared amount of Benzoyl Peroxide.

12. Failure to limit access to drug product labels. [21 CFR 211.122(d)]. Access to labels, which are stored in the production room on shelves and in cabinets, is not limited to authorized personnel.

13. Failure to identify all compounding and storage containers, processing lines, and major equipment used during production. [21 CFR 211.105 (a) and (b)] During the inspection our investigator observed that manufacturing equipment containing product was unidentified as to contents and phase of processing.

14. Failure to evaluate, at least annually, by record review the quality standards of each drug product to determine the need for changes in specifications, manufacturing or control procedures. [21 CFR 211.180(e)]

15. Failure to retain reserve samples representative of each lot of each shipment of each active ingredient. [21 CFR 211.170(a)]

In addition, the investigator noted that several activities associated with drug manufacturing were conducted in undefined areas of the same room, including weighing of materials, compounding of drug product, mixing of drug product, filling of product in final containers, and labeling of finished products. Furthermore, the same undivided room was also partially used to assemble metal and cardboard racks for another division of the firm not related to the manufacture of the firm's drug products. Be advised that each operation in the drug manufacturing process shall be separate and in defined areas, or the firm shall have other such controls to prevent contamination or mix-ups.

The above identification of violations and the observations on the form FDA-483 issued at the end of the inspection are not intended to be an all-inclusive list of violations. It is your responsibility to assure adherence with each requirement of the Current Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering award of contracts. Additionally, any pending NDAs, ANDAs, or export approval requests may not be approved until the above violations are corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions include seizure and/or injunction.

You should notify this office in writing, within 15 working days of the receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for delay and the time within which corrections will be completed.

Your reply should be sent to Compliance Branch, Food and Drug Administration, New York District, 158-15 Liberty Avenue, Jamaica, NY 11433, Attention: Laurence D. Daurio, Compliance Officer.

Sincerely,

Jerome G. Woyshner
District Director